REMARKS

Claims 7, 20, 21, and 28-39 are pending in the application. Claims 1-6, 8-14, and 22-27 have been cancelled without prejudice.

New claims 34-39 have been added, but do not incorporate new matter. New claim 34 is a rewritten version of claim 4 (which indirectly depended from claim 1 via claim 3) that incorporates within it the elements of claim 6. Similarly, new claim 35 is a rewritten version of claim 25 (which indirectly depended from claim 23 via claim 24) that incorporates the elements previously recited in dependent claim 27. Support for each of the new claims is found at least in the Specification at page 3, lines 17-19; page 4, lines 11-14; and claims 1-22 as originally filed.

Claims 7, 20, 21, 28, and 30-32 have been amended to correct claim dependencies in view of the rewritten versions of the claims submitted herein.

In Paper No. 11, the Examiner indicated the claims 4, 6, 7 and 27 were allowable. Claims 4, 6, and 27 have been cancelled; however, the subject matter of these claims has been incorporated into claims 34 and 35.

This Amendment is submitted in accordance with the Revised Amendment Format permitted by Pre-OG Notice "Amendments in Revised Format Now Permitted," dated January 31, 2003.

A copy of the pending claims in the order preferred by the applicants is submitted herewith for the Examiner's convenience.

I. Claim Objections - Improper Dependent Form.

In Paper No. 11, the Examiner has objected to claims 8-14 and 30 under 37 C.F.R. 1.75(c). Claims 8-14 have been cancelled by the Amendment. Claim 30 has been amended to depend from claim 35, which recites a "Composition comprising . . .". Accordingly, the Examiner's objection is no longer applicable. It is respectfully requested that the Examiner reconsider and withdraw the objection.

II. Claim Objection - Duplicate Claims.

The Examiner has objected to claims 8 and 30 asserting that such claims are considered to be substantially duplicative. Claim 8 has been cancelled; therefore, it is submitted that the Examiner's objection is no longer applicable. Its reconsideration and withdrawal is respectfully requested.

III. Rejection Under 35 U.S.C. § 112, First and Second Paragraphs.

At page 3, the Examiner has rejected claims 5 and 26 under 35 U.S.C. § 112, first and second paragraphs, on various grounds. Claims 5 and 26 have been cancelled, and the language to which the Examiner objected has not been incorporated into any of the pending claims. Accordingly, the Examiner's § 112 rejections are no longer applicable. It is requested that the Examiner reconsider and withdraw the rejections based upon § 112, first and second paragraphs.

IV. Rejection under 35 U.S.C. § 102(e) Based upon U.S. Patent No. 6,120,803.

At page 4, the Examiner has maintained the rejection of claims 1-3, 14, 20-22, 30, and 33 under 35 U.S.C. § 102(e) as being anticipated by U.S. Patent No. 6,120,803 of Wong et al. ("Wong"). The Examiner asserts that the recitation of a broad category of excipients that "increases the solubility of fexofenadine or its salts" does not carry any patentable weight. However, the Examiner notes that if applicants recite specific excipients, the claims would be distinguishable from Wong, and therefore allowable.

Claims 1-3 and 14 have been cancelled; however, the applicants respectfully traverse this rejection with respect to claims 20-22, 30, and 33, and respectfully request that the rejection not be applied to any of new claims 35-39, for the reasons set forth below.

Wong does not teach each element of the invention as claimed. Wong does not teach a pharmaceutical excipient that increases the solubaility of fexofenadine or the sale of fexofenadine in water, that is one of a cyclodextrin, propylene glycol, or glycofurol (tetraglycol). No disclosure of these excipients is provided in Wong, (see, e.g. Col. 6 where excipients are disclosed), nor is there any indication that it would be desirable to select the recited excipients that act to increase the solubility of fexofenadine or its salts for use in the Wong composition.

Additionally, Wong does not teach a composition adapted for delivery of fexofenadine or a pharmaceutically acceptable salt to the eye or nose. Wong teaches a composition in the form of a banded capsule, which must be immersed in liquid for a long period of time in order for the fexofenadine to be released from the composition. Wong teaches that such compositions are for oral administration, not a suitable dosage form for intranasal or intraocular use.

Accordingly, for at least the reasons given above, Wong does not disclose each element of the invention, and therefore does not render it anticipated under 35 U.S.C. § 102(e). It is respectfully requested that the Examiner reconsider and withdraw the rejection.

V. Rejection under 35 U.S.C. § 102(e) Based Upon U.S. Patent No. 6,027,746.

The Examiner has maintained his rejection of claims 1-3, 12-14, and 20 under 35 U.S.C. § 102(e) as being anticipated by U.S. Patent No. 6,027,746 of Lech ("Lech"). As noted above, claims 1-3, and 12-14 have been cancelled. Claim 20 is pending. The applicants respectfully traverse the rejection with respect to claim 20 and request that the Examiner not apply the rejection to new claims 35-39.

Lech teaches a pharmaceutical delivery system comprising a chewy, soft gelatin capsule within which a drug adsorbate is dispersed in a solid or liquid fill material. Lech teaches that fexofenadine may be adsorbed onto flake-like particles of an adsorbate, then incorporated into the chewy capsule. Because the drug is adsorbed onto the flake-like material, it is prevented from dissolving into the liquid or solid excipient. This drug adsorbable complex is critical to the Lech composition. Because the active agent is prevented from dissolving the stated goal of Lech

is accomplished -- the patient does not experience the bitter taste of the drug when administered orally.

Lech does not teach each element of the invention, as it does not teach a pharmaceutical excipient that increases the solubility of fexofenadine in water that is a cyclodextrin, propylene glycol, and glycofurol (tetraglycol). There is no discussion in Lech of any efforts to increase or solubilize the fexofenadine in water or in any other solvent. In fact, the composition of Lech is expressly directed to avoiding the solubilization of fexofenadine. Thus, because Lech does not teach a pharmaceutical excipient that increases the solubility of fexofenadine in water that is a cyclodextrin, propylene glycol, or glycofurol (tetraglycol), it does not anticipate the invention as claimed.

In view of the foregoing, it is respectfully requested that the Examiner reconsider and withdraw the rejection based upon Lech.

VI. Rejection Under 35 U.S.C. § 102(e) Based Upon U.S. Patent No. 6,117,452.

The Examiner has maintained the rejection of claims 1-3, 12-14 and claim 20 under 35 U.S.C. § 102(e) as being anticipated by U.S. Patent No. 6,117,452 of Ahlgren et al. ("Ahlgren"). Claims 1-3 and 12-14 have been cancelled. However, the applicants traverse the rejection with respect to claim 20, and request the Examiner not apply the rejection to new claims 35-39.

Ahlgren does not teach each element of the invention. The invention of claim 20 is a method of treating a patient with fexofenadine or a pharmaceutically acceptable salt. The method includes administering an effective amount of a composition that consists essentially of fexofenadine or a pharmaceutically acceptable salt and a pharmaceutical excipient which increases the solubility of fexofenadine or its salt in water that is selected from the group consisting of a cyclodextrin, propylene glycol, and glycofurol (tetraglycol). Ahlgren, in contrast, teaches excipients that are water-insoluble, and therefore would necessarily not serve to increase the solubility of fexofenadine in water. Further, the water insoluble excipients taught in Ahlgren do not include cyclodextrin, propylene glycol, and glycofurol (tetraglycol).

Accordingly, for at least the reasons set forth above, it is respectfully submitted that Ahlgren does not teach each element of the claimed invention. Therefore it does not anticipate the invention; reconsideration and withdrawal of the rejection of the § 102(e) rejection based upon Ahlgren is respectfully requested.

VII. Rejection Under 35 U.S.C. § 102(a) Based Upon the PDR, Pages 1189-1190.

The Examiner has maintained the rejection of claims 1-3, 9-11, 14, 20-22, and 33 under 35 U.S.C. § 102(a) asserting that these claims are anticipated by pages 1189 to 1190 of the Physicians' Desk Reference (PDR), 52nd Ed. 1998. Claims 1-3, 9-11, 14, and 22 have been cancelled. However, the applicants traverse the rejection with respect to the remaining claims, and request it not be applied any of the new claims.

The PDR discloses ALLEGRA™, a pharmaceutical formulation containing fexofenadine hydrochloride formulated as capsules for oral administration. According to the PDR each capsule contains 60 milligrams of fexofenadine hydrochloride and croscamellose sodium, gelatin, lactose, microcrystalline cellulose, and pre-gelatinized starch.

In contrast, the invention is a composition that includes a pharmaceutical excipient that increases the solubility of the fexofenadine or its salt in water that is selected from the group consisting of a cyclodextrin, propylene glycol, and glycofurol (tetraglycol). The PDR does not teach use of any of the recited excipients. Therefore, for at least this reason, the PDR does not teach each element of the invention. Accordingly, it is respectfully requested that the Examiner reconsider and withdraw the rejection based upon the PDR.

VIII. Rejection Under 35 U.S.C. § 102(e), or Alternatively, Under 35 U.S.C. § 103(a) Based Upon Wong.

At page 7 of Paper No. 11, the Examiner has rejected claims 5, 8, and 30 under 35 U.S.C. § 102(e) as anticipated by or, in the alternative, under 35 U.S.C. § 103(a) as obvious over the Wong reference. Claims 5 and 8 have been cancelled and the subject matter of each has not been incorporated into any of the presently pending claims. Therefore, the rejection is rendered inapplicable. However, the applicants traverse the rejection with respect to claim 30, and further request that it not be applied to any of the new claims.

Wong does not anticipate the invention of claim 30 for the reasons discussed in Section IV above. Specifically, Wong does not teach a composition comprising fexofenadine or a pharmaceutically acceptable salt thereof and a pharmaceutical excipient that increases the solubility of fexofenadine or its salt in water that is selected from a cyclodextrin, propylene glycol, and glycofurol (tetraglycol).

Additionally, the disclosure of Wong does not render claim 30 obvious, as it does not teach or suggest each element of the invention. Wong does not teach or suggest use of an excipient that is one of a cyclodextrin, propylene glycol, or glycofurol (tetraglycol). Nor would a person of skill in the art have been motivated to modify Wong to arrive at the invention by substituting the recited excipients for those of Col. 6 of Wong.

Accordingly, it is respectfully requested that the Examiner reconsider and withdraw the rejection of claim 30 under 35 U.S.C. § 102(e), or in the alternative, under 35 U.S.C. § 102(a).

IX. Rejection Under 35 U.S.C. § 103(a) Based Upon the PDR.

The Examiner has rejected claims 23, 24, 26, 28, 31, and 32 under 35 U.S.C. § 103(a) as being unpatentable over PDR (pages 1189 to 1190). As discussed above, claims 23, 24, and 26 have been cancelled. However, the applicants traverse this rejection with respect to claims 28, 30 and 32, and request that it not be applied to any of new claims 34-39.

As discussed in Section VII of this Response, the PDR discloses a fexofenadine hydrochloride formulation in capsule form containing croscamellose sodium, gelatin, lactose, microcrystalline cellulose, and pre-gelatinized starch. Unlike the invention as claimed, the PDR does not teach or suggest use of a pharmaceutical excipient that increases the solubility of fexofenadine or salts in water that is selected from the group consisting of a cyclodextrine, propylene glycol, and glycofurol (tetraglycol). Therefore, the Examiner has not established a case of *prima facie* obviousness for the PDR does not teach or suggest element of the invention. Additionally, a person of ordinary skill would have had no motivation to modify the disclosure of the PDR to arrive at the present invention. ALLEGRA™ is an oral formulation; the invention is a composition adapted for delivery to the eye or nose.

Accordingly, it is respectfully requested that the Examiner reconsider and withdraw the § 103 rejection based upon the PDR.

X. Rejection Under 35 U.S.C.§ 103(a) Over U.S. Patent No. 5,691,370.

At page 8-9, the Examiner has rejected claims 23-26, 28-29, 31, and 32 under 35 U.S.C. § 103(a) over U.S. Patent No. 5,691,370 of Cupps et al. ("Cupps"). As basis for the rejection, the Examiner asserts that Cupps discloses a pharmaceutical composition that comprises terfenadine or terfenadine carboxylate, and carriers such as lactose, sucrose, starches, propylene

glycol, glycerin, and mannitol. While the specific amounts of fexofenadine recited in the claims are not disclosed in Cupps, the Examiner argues that such difference does not render the claims patentable as it would have been obvious to one of ordinary skill in the art at the time the invention was made to optimize the composition of Cupps through routine experimentation to achieve the amount of fexofenadine that is recited. The applicants respectfully traverse the rejection for the reasons set forth below, and further request that the rejection not be applied to the new claims.

Cupps discloses a composition containing specific substituted 5-(2-imidazolinylamino) benzimidazole compounds that are alpha adrenoreceptor agonists in combination with other active agents, such as terfenadine, and other excipients, such as sugars, polysaccharides, wetting agents, emulsifiers, stabilizers, antioxidants, and preservatives. Cupps teaches an appropriate dosage of terfenadine, if a composition containing terfenadine is to be administered patient, but does not teach or suggest the specific amount of terfenadine present in the 5-(2-imidazolinylamino)benzimidazole composition.

The invention of claims 34, 7, 20, 21 is a composition that consists essentially of fexofenadine or a pharmaceutically acceptable salt thereof and a pharmaceutical excipient that is a cyclodextrin, propylene glycol, and glycofurol (tetraglycol). The composition is adapted for delivery of the fexofenadine or pharmaceutically acceptable salt thereof to the eye or nose.

In contrast, Cupps requires that the composition contain at least the specified 5-(2-imidazolinylamino)benzimidazole compound, regardless of whether the terfenadine is or is not present. Thus, a person of skill in the art would not have been motivated to make the modification suggested by the Examiner. Namely, the person of skill would not have removed the substituted 5-(2-imidazolinylamino)benzimidazole compound from the Cupps composition, for to do so would be to render the Cupps reference useless for its intended purpose.

The invention of claims 35, 28-33 and 36 is a composition comprising fexofenadine or a pharmaceutically acceptable salt and a pharmaceutical excipient that is a cyclodextrin, propylene glycol or glycofurol (tetraglycol). The fexofenadine or pharmaceutically acceptable salt is present in an amount selected from 100 μg/ml to 100 mg/ml and .05% to 40% wt/wt.

Cupps described compositions that comprise certain substituted 5-(2-imidazolinylamino)benzimidazole compounds, a pharmaceutically acceptable carrier and, optionally, an antihistamine such as terfenadine carboxylate. The carrier may be any compatible

solid or liquid filler dilutant or encapsulating substance that is suitable for administration to a human. The list of suitable carriers provided in Cupps includes propylene glycol. Cupps teaches that the compositions may be administered perorally, or topically, for example, as intranasal doses or eye drops.

However, Cupps neither teaches nor suggests a composition that contains an excipient selected from a cyclodextrin and glycofurol (tetraglycol). Additionally, there is no teaching in Cupps to provide a composition that is adapted for delivery to the eye or nose.

Further, there is nothing in Cupps to suggest providing a composition that is adapted for delivery to the eye or to the nose that specifically contains propylene glycol as the excipient. In fact, the teachings of Cupps would have actively discouraged the skilled person from including propylene glycol in a composition that is adapted for the eye or nose. Cupps teaches that propylene glycol is suitable for use as a carrier in peroral compositions, i.e., non in compositions adapted for delivery of a drug to the eye or to the nose, see Col. 17, lines 48-58. Moreover, the only compositions in Cupps that include propylene glycol are those that are specifically identified as oral formulations. See examples H, Q, and R.

There is no teaching or suggestion in Cupps to provide a composition that comprises fexofenadine or a pharmaceutically acceptable salt thereof that is adapted for delivery to the eye or nose. Still less is there any teaching in Cupps as to the amount of fexofenadine or pharmaceutically acceptable salt to be included in the composition. There is nothing in Cupps to suggest providing a composition that comprises fexofenadine or a pharmaceutically acceptable salt in the amount specified in the claims in combination with an excipient that is a cyclodextrin, glycofurol (tetraglycol) or propylene glycol. Thus, the teaching in Cupps would not have led, motivated, or otherwise instructed a person of skill to provide a composition according to the invention as claimed.

Accordingly, for at least the reasons given above, it is respectfully submitted that the Examiner has failed to establish a *prima facie* case of obviousness based upon the Cupps reference. Consequently, it is requested that the Examiner reconsider and withdraw the § 103 rejection based upon Cupps.

CONCLUSION

In view of the foregoing, it is respectfully submitted that the pending claims 7, 20, 21, 28-39 are distinguishable over the cited art. Accordingly, the Examiner's reconsideration and allowance of the claims at the earliest opportunity is earnestly solicited.

Respectfully submitted,

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20 march 2003 By: Kristyne a. Bullock
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PENDING CLAIMS IN ORDER PREFERRED BY APPLICANT
U.S. APPLICATION NO.: 09/8334,312

34. (New) A composition consisting essentially of

(i) fexofenadine or a pharmaceutically acceptable salt thereof and

(ii) a pharmaceutical excipient that increases the solubility of the fexofenadine or salt in water selected from the group consisting of a cyclodextrin, propylene glycol, and glycofurol (tetraglycol),

which composition is adapted for delivery of the fexofenadine or pharmaceutically acceptable salt thereof to the eye or nose.

7. (Amended) A composition as claimed in claim 34~~Claim 6~~, wherein the cyclodextrin is hydroxypropyl-β-cyclodextrin.

20. (Amended) A method of treating a patient in need of treatment with fexofenadine or a pharmaceutically acceptable salt thereof which comprises administering an effective amount of a composition according to ~~Claim 1~~claim 34 to a patient in need of such treatment.

21. (Amended) A method of treating rhinitis which comprises administering an effective amount of a composition according to ~~Claim 1~~claim 34, to a patient in need of such treatment.

35. (New) A composition comprising

(i) fexofenadine or a pharmaceutically acceptable salt thereof in an amount selected from the group consisting of 100 μg/ml to 100 mg/ml and 0.5% to 40% wt/wt and

(ii) a pharmaceutical excipient that increases the solubility of the fexofenadine or salt in water selected from the group consisting of a cyclodextrin, propylene glycol, and glycofurol (tetraglycol),

which composition is adapted for delivery of the fexofenadine or pharmaceutically acceptable salt thereof to the eye or nose.

28. (Currently amended) The composition as claimed in claim 35~~claim 23~~, which further comprises a gelling agent or a bioadhesive material.

38. (New) The composition of claim 28, wherein the gelling agent or bioadhesive material is a polysaccharide.

29. (Previously added) The composition as claimed in claim 28, wherein the gelling agent or bioadhesive material is selected from the group consisting of pectin, alginate, starch, gellan, chitosan, and a block co-polymer.

39. (New) The composition of claim 29, wherein the block co-polymer is a poloaxmer.

30. (Currently amended) The composition as claimed in claim 35~~claim 1~~, which further comprises a material that provides for controlled release of the fexofenadine or a pharmaceutically acceptable salt thereof.

36. (New) The composition of claim 35, wherein the cyclodextrin is hydroxypropyl-β-cyclodextrin.

37. (New) The composition of claim 35, wherein the composition further comprises an aqueous vehicle.

31. (Currently amended) A method of treating a patient in need of a treatment with fexofenadine or a pharmaceutically acceptable salt thereof, the method comprising administering an effective amount of the composition according to claim 35~~claim 23~~ to a patient in need of such treatment.

32. (Currently amended) A method of treating rhinitis, the method comprising administering an effective amount of a composition according to claim 35~~claim 23~~ to a patient in need of such treatment.

33. (Previously added) A method of treating a patient with a controlled release dose of fexofenadine or a pharmaceutically acceptable salt thereof, the method comprising

administering an effective amount of a composition according to claim 30 to a patient in need of such treatment.

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